Our attention need hardly be directed to the fact that the Departments of Pharmacy, Chemistry and Materia Medica offer a wealth of material for the duplication, repair and construction of standard or special apparatus.

EXTRACTION OF NUX VOMICA IN THE MAKING OF TINCTURE.*

BY NELLIE PERRY WATTS.[1]

When the Tincture of Nux Vomica, manufactured according to the directions of the United States Pharmacopœia, Eleventh Revision, came upon the market, great indeed was the consternation. For decades this tincture had been an amber solution; the new product, however, is a red liquid. Not only is it red, it is of different shades of red; the products of the various manufacturers differ in shade, and even one lot of a manufacturer may vary from his next lot. You well know the doubt this change in color causes in the minds of the retail and dispensing pharmacists, particularly in the refilling of prescriptions calling for this galenical.

The formula for preparing the Tincture of Nux Vomica has changed many times. In reviewing its history in this country it will be found that *until the* Third Revision in 1851 the crude drug (nux vomica) only was official. In the revision of 1851 the tincture was directed to be made from the rasped seed, using eight ounces to two pints of finished tincture. The drug could be macerated, or macerated and later percolated, with the then official alcohol, specific gravity 0.835, which was about 90 per cent by volume. A menstruum of alcohol, too, yields an amber-colored tincture. For several decades no changes were made in this preparation, other than that the rasped drug was replaced by a fine powder. In the Sixth Revision, among other changes the menstruum was diluted—eight parts of alcohol to one part of water. It was in 1890, the Seventh Revision of the Pharmacopœia, that acid was first introduced; and extract of nux vomica was made from 1000 Gm. of drug, 50 cc. of acetic acid, 750 cc. of alcohol and 250 cc. of water. The tincture was made by dissolving sufficient of the extract in a mixture of alcohol and water (3:1) to have a concentration of 0.3 per cent of alkaloids. In the Ninth Revision (1910) the tincture was again made by percolating the drug without acid; in 1920 the process was continued with the addition of acetic acid. In the Eleventh Revision the 10 cc. of acetic acid per 100 Gm. of drug was replaced by 7.5 cc. of hydrochloric acid.

Nux Vomica seeds contain the alkaloids strychnine and brucine combined with igasuric acid, an acid similar to tannic acid. There is also present a glucoside —loganin (1).

In a study of this tincture five experimental lots were prepared; in each instance 100 Gm. of nux vomica, ground to a moderately coarse powder, was packed in a glass percolator and, after being moistened with the menstruum for twenty-four hours, drained at a rate of 3 to 5 drops per minute. Percolation was continued until the tincture measured 1000 cc. The menstrua used were:

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1. Alcohol, 3 parts, distilled water, 1 part.
2. Alcohol, 150 cc.; distilled water, 42.5 cc.; hydrochloric acid 7.5 cc. Completed with alcohol, 3 parts; distilled water, 1 part.
3. Alcohol, 150 cc.; distilled water, 45 cc.; hydrochloric acid, 5 cc. Completed with alcohol, 3 parts; distilled water, 1 part.
4. Alcohol, 150 cc.; distilled water, 40 cc.; hydrochloric acid, 10 cc. Completed with alcohol, 3 parts; distilled water, 1 part.
5. Alcohol, 750 cc.; distilled water, 240 cc.; acetic acid, 10 cc. Completed with alcohol, 3 parts; distilled water 1 part.

The drug moistened by menstrua numbers 1 and 5 was of a gray color, while that moistened by numbers 2, 3 and 4 was of a pink shade. In all cases practically all of the heavily colored portion of the tincture was to be found in the first 200 cc. of the percolate. In the filtering of these percolates, after chilling them at 5° C. over night, tincture number 1 filtered easily, number 5 the next easily and the three containing hydrochloric acid with difficulty. This was true when an ordinary funnel was used and also when a Büchner was employed. The finished tinctures 1 and 5 were amber liquids, while numbers 2, 3 and 4 (those containing hydrochloric acid) were red.

When these tinctures were assayed for their strychnine content, all were found to come within the Pharmacopœial range of 0.108 to 0.120 per cent. Number 2 (U. S. P. XI) gave a slightly higher yield; numbers 1, 3 and 5 were of practically the same strength; and number 4 (10 cc. of hydrochloric acid) was shown to be slightly weaker than the others.

In a total solids assay, in which 10 cc. of each tincture was evaporated to dryness at 100° C., the U. S. P. XI product gave the most residue. Of more interest than the weight, however, is the nature of this residue. In the cases where hydrochloric acid had been in the menstruum a black residue with a tarry or phenolic odor resulted, while an amber-color residue almost lacking in odor resulted when hydrochloric acid was not used.

Why is the tincture official at present red? As a possible explanation I offer that the glucoside loganin is hydrolyzed in the presence of the hydrochloric acid, yielding glucose and a red substance. In the literature it is recorded that loganin turns red in the presence of sulfuric acid (2). The ground nux vomica turns pink when moistened with sulfuric acid and with hydrochloric acid, but not with acetic acid.

By the use of Fehling's solution to detect the presence of glucose, and in turn the hydrolysis of a glucoside, it was found that in tinctures 1 and 5 no reduction occurred, while in the tinctures containing the hydrochloric acid the Fehling's solution was reduced.

The method of preparation of this tincture is now before the Committee of Revision of the United States Pharmacopœia. In a *Bulletin*, dated August 13, 1937, a paragraph referring to this tincture reads:

"The Contact Committee and others believe the U. S. P. X acetic acid menstruum should be reinstated as the new hydrochloric acid menstruum produces color and other changes."

REFERENCES.

(1) United States Dispensatory, 22nd Edition, page 705; National Dispensatory, 3rd Edition, page 1054; King's American Dispensatory, 19th Edition, page 1314.

(2) Rosenthaler, L., *Schweiz. Apoth.-Ztg.*, 61, 399 (1923).